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Original Article

OBSERVATIONAL STUDY ON THE INCIDENCE OF ADVERSE DRUG REACTIONS TO FIRST LINE ANTIRETROVIRAL AGENTS IN MELANESIANS ADULT HIV/AIDS PATIENTS

ZAKKY CHOLISOH[1*], SITI SITATUL MARAH[1], BURHANNUDIN ICHSAN[2]

[1]Faculty of Pharmacy, Universitas Muhammadiyah Surakarta, Central Java, Indonesia. [2]Faculty of Medicine, Universitas Muhammadiyah Surakarta (UMS), Jalan Ahmad Yani, Sukoharjo-57169, Central Java, Indonesia
[*]Corresponding author: Zakky Cholisoh; [*]Email: zakky.cholisoh@ums.ac.id

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ABSTRACT

Objective: Acquired immunodeficiency syndrome is a disease caused by Human Immunodeficiency Virus (HIV), and antiretroviral combinations are the mainstay therapy for HIV/AIDS patients. Common problems in using antiretroviral drugs (ART) are Adverse Drug Reactions (ADRs), which can affect the treatment of HIV patients. ADRs has strong genetic predisposition. This research was conducted to determine the profile and prevalence of ADRs in Melanesians HIV patients who use first-line ARTs.

Methods: This was observational research, which descriptively present the highest prevalence of adverse drug reactions in Melanesians' patients with antiretroviral medications. The inclusion criteria were Melanesians adult patients with HIV/AIDS who had high adherence in using first-line ARTs and willing to be interviewed by filling informed consent. Exclusion criteria were patients with unstable conditions. Patients were followed for 1 mo. Data of perceived adverse drug reactions which the patients had experienced in 1 mo was collected through interviews with data collection carried out every week.

Results: Of total 143 Melanesian patients on antiretroviral, the number of patients who experienced adverse drug reactions there were 142 (99.3%) and 1 (0.7%) patient who did not experience ADRs. Of the 645 side effects experienced by patients included dizziness 244 (37.8%), nausea 164 (25.4%), drowsiness 79 (12.2%), hepatotoxicity 56 (8.7%), vomiting 36 (5.6%), difficulty sleeping 36 (5.6%), anemia 15 (2.3%), weight loss 8 (1.2%), itchy spots 3 (0.5%), hallucinations 2 (0.3%), and myalgia 2 (0.3%).

Conclusion: The incidents of adverse drug reactions among Melanesians patients on antiretroviral were prevalent on 99.3% of patients with dizziness, nausea, and drowsiness as the most commonly perceived adverse drug reactions. The results highlight the urgent need for routine monitoring and early detection of ADRs in this population. These findings also suggest the importance of individualized treatment plans and potential pharmacogenetic considerations to improve tolerability and adherence. Clinicians should also be equipped with targeted education and management strategies to mitigate the impact of ADRs on long-term treatment outcomes.

Keywords: Adverse drug reactions, Antiretroviral, HIV, AIDS

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INTRODUCTION

In 2020, the World Health Organization reported that 37.7 million individuals globally were living with HIV, with 680,000 fatalities attributed to the virus, and 73% of those infected were taking antiretroviral medication [1]. As of March 2022, 34 provinces in Indonesia have supplied the most recent data. From January to March 2022, 10,525 individuals living with HIV (PLHIV) were identified among 941,973 individuals tested for HIV, with 8,784 individuals receiving antiretroviral (ART) treatment, or 83.4%. The five provinces with the highest reported AIDS cases, in descending order, are Central Java, Bali, Papua, East Java, and South Sulawesi [2].

In the initial two decades, this epidemic saw significant transformation with the advent of antiretroviral medication (ART). Individuals with HIV/AIDS (PWH) can lead more productive lives provided they comply with the prescribed antiretroviral therapy (ART) regimen [3]. Antiretroviral therapy is a lifelong treatment for those with HIV/AIDS involving the continuous administration of drugs. The objective is to inhibit HIV replication within the body [4]. The medication required to maximally suppress the viral replication is 90%-95% of all doses [5].

Antiretroviral therapy has demonstrably decreased the mortality rate associated with HIV infection, converting it from a swiftly lethal disease into a tolerable chronic condition conducive to long-term life [6, 7]. The Joint United Nations Program on HIV and AIDS (UNAIDS) established the 90-90-90 initiative, which aims to detect 90% of those living with HIV worldwide, provide treatment to 90% of those diagnosed, and attain viral suppression in 90% of those receiving treatment by 2020 [8]. The advancement of antiretroviral medications has markedly transformed the perspective of HIV/AIDS from a perilous illness to a chronic condition. When effectively controlled, it can reduce mortality and morbidity while enhancing quality of life [9].

The high and increasing global and national ART coverage demonstrates the success of treatment scale-up. However, the growing use of ART is also accompanied by rising concerns regarding adverse drug reactions (ADRs), which can compromise adherence and clinical outcomes. As ART is a lifelong therapy, consistent patient engagement remains critical-yet many patients still demonstrate low levels of adherence [10, 11]. Like all pharmacological therapies, ART can cause adverse effects [12], with ADRs classified as a major category of drug-related problems (DRPs) that can hinder the delivery of effective pharmaceutical care.

According to the World Health Organization (2023), ADRs are defined as harmful, unintended, or undesirable effects of medications administered at normal doses for prevention, diagnosis, or treatment purposes [13]. ADRs are a major contributor to morbidity and mortality [14], and a strong correlation exists between ADR occurrence and genetic predisposition [15]. ADRs associated with antiretroviral medications have been increasingly linked to genetic variations that affect drug metabolism, transport, and immune responses. For instance, hypersensitivity to abacavir has been strongly associated with the presence of the HLA-B*57:01 allele, leading to a potentially life-threatening reaction in genetically predisposed individuals. This association has been so well-established that pharmacogenetic screening for HLA-B57:01 is now recommended before initiating abacavir therapy [16]. Similarly, variations in CYP2B6, a key enzyme involved in the metabolism of efavirenz, have been shown to influence plasma concentrations of the drug. Individuals carrying the CYP2B6*6 allele tend to have slower metabolism, leading to elevated efavirenz levels and increased risk of central nervous

system-related ADRs such as dizziness, vivid dreams, and mood disturbances [17]. These findings highlight the need for considering genetic factors in the management of ART, especially in diverse populations like Melanesians, where specific allele frequencies may differ and influence susceptibility to ADRs.

Drug-induced morbidity and mortality thus present ongoing challenges in clinical pharmacy practice. Pharmacists significantly contribute to the efficacy of a treatment. A primary responsibility of a pharmacist is to deliver patient-centered pharmaceutical services, referred to as Pharmaceutical Care [18]. In patient medication therapy, a pharmacist is required to recognize drug-related problems that have arisen or may arise. The decrease in the occurrence of Adverse Drug Reactions (ADRs) can enhance patient compliance with medication [19].

The quarterly report on HIV/AIDS development for the third quarter of 2022 indicates a rise in the number of HIV/AIDS patients at regional hospital in Central Papua. This has led researchers to investigate the occurrence of adverse medication responses in Antiretroviral (ART) therapy among Melanesians HIV/AIDS patients, as research of adverse drug reactions profiles in this subset is very limited.

MATERIALS AND METHODS

Research design and location

This study has obtained approval from the ethic committee of Dr. Moewardi Surakarta Hospital, with reference number 609/IV/HREC/2023. This study is using an observational descriptive design involving Melanesians patients who attended the attended the Voluntary Counseling and Testing (VCT) service at the Central Papua Regional Hospital in 2023. The data encompassed sociodemographic, clinical factors, and antiretroviral (ART) use profiles. The study population consisted of adult Melanesian individuals living with HIV who were receiving first-line ART and met the predefined inclusion and exclusion criteria. All participants were confirmed to have a good level of adherence, defined by a Medication Possession Ratio (MPR) greater than 95%, [20] and had access to medication adherence support services provided by the hospital.

Data collection

Data recorded in the data collection sheet included demographic information, clinical factors such as comorbidities and opportunistic infections, and medication-related factors including the antiretroviral regimen profile, duration of ART use, and concurrent medication usage. Comorbidities and opportunistic infections were verified based on documented diagnoses in the patients' medical records.

The inclusion criterion was adult patients who were willing to participate in the study, confirmed by completing and signing an informed consent form. The exclusion criteria included unstable mental illnesses shown in medical records, as they were deemed to impair the ability to provide information regarding perceived ADRs. Consequently, 143 patients were chosen as the study population. The sample size in this investigation was calculated using the proportion-based formula established by Lemeshow *et al.* [21].

$$n = \frac{N\ Z^2 1-\alpha/2pq}{d^2(N-1) + Z^2 1-\alpha/2pq}$$

$$n = \frac{430\ x\ 1{,}96^2\ x\ 0{,}867\ (1-0{,}867)}{0{,}05^2 x\ (430-1) + 1.96^2\ \ 0{,}867\ (1-0{,}867)}$$

n = 125.33 ≈ 126+10% = 138.6 ≈ 140 samples

Where:

n = quantity of samples

N = population size

$Z^2 1-\alpha$ = standard normal distribution values (Z-table) at 95% confidence level (1.96)

P = projected population proportion of 86.7% [22].

q= 1 – P (1-0,867 = 0,133)

d= acceptable absolute mistakes (0.05)

The calculation produced a minimum of 140 samples. An additional 10% was included in the calculated sample size to account for potential attrition or incomplete data during the study period.

Table 1: Sociodemographic, clinical, and medications characteristics of HIV/AIDS Melanesians patients who experienced ADRs on antiretroviral (n = 142)

Patients' characteristics		Freq., percentage (%)
Age (y)	12-35 y	129 (90.8)
	≥36 y	13 (9.2)
Gender	Male	75 (52.5)
	Female	67 (47.5)
Marital status	Married	99 (69.0)
	Unmarried	43 (31.0)
Smoking	Yes	38 (26.8)
	No	104 (73.2)
Alcohol drinking	Yes	29 (20)
	No	114 (80)
Comorbidities	Yes	13 (9.2)
	No	129 (90.8)
Opportunistic infections	Yes	40 (28.2)
	No	102 (71.8)
Type of ART regiment	fixed dose combination (FDC)	93 (65.5)
	Non-FDC	49 (34.5)
The length of ART usage	<6 mo	111 (78.2)
	≥ 6 mo	31 (21.8)

The incidence of ADRs in HIV patients administered first-line ARTs at general hospital in Central Papua during the July-August 2023 timeframe is illustrated in table 2.

Assessment of adverse drug reactions (ADRs) and data analysis

This study examines sociodemographic, clinical factors, antiretroviral (ART) regiment profiles, and the incidence of adverse drug reactions (ADRs). The initial interview aimed to identify ADRs and was conducted when individuals attended the Voluntary Counseling and Testing (VCT) service during which information on patient characteristics, clinical characteristics, and ART prescribing and usage profiles was acquired utilizing patient's data collecting forms and medical records. The second to fourth interviews were conducted weekly via telephone, utilizing the same questionnaire to identify any occurrences of adverse drug reactions (ADRs).

Patients were followed for 1 mo. Data on perceived adverse drug reactions (ADRs) experienced during this period were collected through weekly interviews and assessed using Naranjo Algorithm

[23]. The 1 mo observation period was selected to capture recent or persistent ADRs that may still impact adherence and quality of life. Regular weekly follow-up allowed for timely identification and documentation of ongoing or recurrent ADRs, providing a practical snapshot of the current burden of drug-related adverse effects in this population. This approach supports the goal of improving clinical monitoring and management strategies, even beyond the initial phase of ART.

RESULTS AND DISCUSSION

The characteristics of patients experiencing adverse drug reactions with antiretroviral data is presented in table 1.

Table 2: Antiretroviral adverse drug reactions characteristics on HIV/AIDS Melanesians patients in Central Papua Regional Hospital (n = 645)

No.	Types of ADRs	Freq., percentage (%)
1	Dizziness	244 (37.8%)
2	Nausea	164 (25.4%)
3	Drowsiness	79 (12.2%)
4	Hepatotoxicity	56 (8.7%)
5	Vomiting	36 (5.6%)
6	Insomnia	36 (5.6%)
7	Anemia	15 (2.3%)
8	Weight loss	8 (1.2%)
9	Skin rash	3 (0.5%)
10	Hallucination	2 (0.3%)
11	Myalgia	2 (0.3%)

DISCUSSION

This study aims to determine the incidence of adverse drug reactions (ADRs) in HIV/AIDS patients receiving first-line antiretroviral therapies (ARTs). Throughout the study period, 143 patients consented to participate in the research. The results encompass sociodemographic data, clinical characteristics, ART usage profiles, incidence rates of ADRs, and the types of ADRs observed. The emergence of adverse drug reactions (ADRs) signifies the inherent intolerance mechanism resulting from the accumulation of drugs deemed harmful. Eluwa's research (2012) concludes that the evaluation and identification of adverse drug reactions (ADRs) is crucial to prevent the manifestation of more severe ADRs [24].

In this study, nearly all patients, totaling 142 (99.3%), experienced adverse drug reactions (ADRs), while only 1 patient (0.7%) did not. These results are comparable to the study conducted by Rukmangathen (2020), where the number of patients with ADRs while using ARTs was greater than those who do not experiencing any ADRs [25]. This study also revealed that the incidence of adverse drug reactions (ADRs) associated with antiretroviral (ART) usage was higher in the male cohort at 52.8%, compared to 47.2% in the female cohort. The results of this study are comparable to those conducted by Khan in 2016 [26].

The incidence of adverse drug reactions (ADRs) associated with antiretroviral (ART) medications was notably higher among younger patients aged 12–35 y (n=129) compared to older individuals aged 36–65 y (n=13). These findings contrast with Mendes' (2018) study [22], which reported that the risk of ADRs may increase with age. This discrepancy may be explained by differences in population characteristics, particularly genetic variations that may affect drug metabolism in Melanesians, a population that remains underrepresented in pharmacogenomic studies. Other contributing factors may include differences in ART regimens, variations in nutritional status, and the presence of comorbidities. Additionally, disparities in pharmacovigilance practices, follow-up duration, and sample sizes between studies may account for the observed differences in ADR patterns.

Similarly, with respect to employment status, ADRs were more common among working patients (71.8%) than non-working patients (28.2%), a trend contrary to Tadesse's (2014) report, which showed fewer ADRs among employed individuals [27]. This variation may be influenced by behavioral factors such as increased stress, irregular medication schedules, or reduced healthcare access among working individuals in our study setting.

The overall ADR prevalence in this study was high (99.3%), which may reflect heightened patient awareness due to adherence support programs, or recall bias, as ADRs were self-reported. The short duration of follow-up is another limitation that may underestimate long-term ADR patterns. Despite these constraints, our findings underscore the importance of routine ADR monitoring, particularly for common symptoms such as dizziness and nausea. Pharmacist-led interventions, including early screening, education, and regular follow-ups, could play a crucial role in improving treatment tolerability and adherence.

The prevalence of adverse drug reactions (ADRs) in smokers is 26.8%, significantly lower than the 73.2% observed in non-smokers. This outcome parallels with the research undertaken by Menezes in 2006 [28]. A nearly same profile of adverse drug reactions (ADRs) is observed in individuals who use alcohol, with a lower incidence of ADRs compared to those who abstain from alcohol consumption. The research by Menezes in 2006 produced analogous findings, indicating the presence of ADRs in the cohort of patients who abstain from alcohol consumption [28].

In this study, approximately 9% of respondents (13 patients) reported comorbidities, while the remaining 91% had no known comorbid conditions. Among the comorbid group, tuberculosis was the most frequently reported condition, and this raises the potential for confounding when evaluating adverse drug reactions (ADRs), particularly hepatotoxicity. While hepatotoxicity is a recognized ADR of antiretroviral therapy (ART), it is also commonly associated with anti-tuberculosis medications such as rifampicin and isoniazid. In fact, rifampicin has been reported to contribute significantly to ADRs, accounting for 28.3% of cases in related studies [29]. Therefore, it is important to consider that in patients with TB co-infection, hepatotoxicity may result from either ART, anti-TB treatment, or their interaction, which complicates attribution. Opportunistic infections, such as hepatitis or tuberculosis, in conjunction with antiretroviral medicine use, elevate the risk of hepatotoxicity [30]. The overlapping toxicity profiles and potential drug-drug interactions highlight the need for close clinical monitoring and liver function testing in patients receiving concurrent therapies.

This study found that the most commonly reported side effects among outpatient with HIV are dizziness (37.8%), nausea (25.4%), and drowsiness (12.2%). These findings are consistent with earlier studies by Arisudhana *et al.*, which reported dizziness (52%) and nausea (47%) as predominant symptoms among outpatient HIV patients [31], and by Barus (2017), who identified nausea or vomiting and dizziness (34.62%) as the most frequent side effects using retrospective data [32]. Comparable patterns were observed in a study by Zosangpuii *et al.* [33] conducted in Northeast India, where gastrointestinal and neurological symptoms, particularly nausea and dizziness, were the most prevalent ADRs associated with

ART. Their study reinforces the idea that certain ADR profiles may be common across diverse populations receiving similar ART regimens. Additionally, skin-related reactions, although less frequently reported in our population, have been recognized in pharmacovigilance research as important manifestations of drug-induced toxicity. A study by Dua *et al.* [34] highlighted the need for awareness and prompt identification of cutaneous ADRs, especially in long-term treatment scenarios involving multiple drug classes.

Notably, more recent studies provide additional support for our results. A 2023 study conducted in Jayapura, Papua, by Adiningsih *et al.* identified dizziness, nausea, and drowsiness as the most common side effects of the Tenofovir-Lamivudine-Efavirenz (TLE) regimen among people living with HIV [35], closely mirroring our findings in a geographically and ethnically similar population. Likewise, a 2021 study at Undata Regional Hospital in Palu, Central Sulawesi, reported dizziness (47%), nausea (12%), and insomnia (15%) as prevalent ADRs in HIV patients on ART [36]. Although these studies do not focus exclusively on Melanesian or Pacific Islander populations, they offer valuable contextual evidence supporting the generalizability of our findings within eastern Indonesian populations. These similarities highlight the need for region-specific pharmacovigilance systems and further investigation into the ADR profiles of ART, particularly in underserved and genetically diverse groups such as the Melanesians.

CONCLUSION

This study concludes that adverse drug reactions (ADRs) among patients on antiretroviral therapy (ART) were highly prevalent, affecting 99.3% of respondents, with dizziness, nausea, and drowsiness being the most commonly reported symptoms. Although the study observed patients over a 1-month period within the context of lifelong ART use, it provides the first insight into the prevalence and pattern of ADRs among Melanesian populations. These findings not only enrich local pharmacovigilance data but also underscore the importance of early identification and management of ADRs to support long-term adherence. Strengthening pharmaceutical care to address ADRs can play a vital role in improving treatment outcomes and supporting global targets such as the UNAIDS 90-90-90 goals—particularly the third “90,” which emphasizes sustained viral suppression through effective and tolerable therapy. Personalized interventions, including routine ADR monitoring and patient-centered counseling, are essential steps toward optimizing ART programs in diverse populations.

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AUTHORS CONTRIBUTIONS

ZC conceptualized and led the research project, supervised the study, and provided critical revisions to the manuscript. BI was guiding the research process and assisting in data interpretation. SSM conducted the experimental work, collected and analyzed the data, and drafted the initial version of the manuscript. All authors reviewed and approved the final manuscript.

CONFLICT OF INTERESTS

Declare none

REFERENCES

1. World Health Organization. HIV/AIDS; 2024. Available from: https://www.who.int/newsroom/factsheets/detail/hiv-aids. [Last accessed on 14 Apr 2025].
2. Director General of Disease Control and Environmental Health. Report on the development of HIV-AIDS and sexually transmitted infectious diseases quarter 1 Jan-Mar 2022. Jakarta. RI: Ministry of Health; 2022. p. 1-23.
3. GBD 2017. HIV collaborators global regional and national incidence prevalence and mortality of HIV, 1980-2017, and forecasts to 2030, for 195 countries and territories: a systematic analysis for the global burden of diseases injuries and risk factors study 2017. Lancet HIV. 2019;6(12):e831-59. doi: 10.1016/S2352-3018(19)30196-1, PMID 31439534.
4. Ministry of Health of the Republic of Indonesia. National guidelines for clinical management of HIV infection and antiretroviral therapy in adults. Jakarta: Ministry of Health RI; 2011.
5. Ministry of Health of the Republic of Indonesia. Pedoman nasional pelayanan kedokteran tata laksana HIV. 2019;1(1):1-220.
6. Utami IT, Prakoeswa FR, Lestari N, Ichsan B. Hubungan tingkat pengetahuan dengan stigma masyarakat terhadap infeksi HIV/AIDS di Indonesia: literature review. J Kedokteran Syiah Kuala. 2023;23(1):99-107.
7. Nugroho C, Kusumaningrum TA. Keyakinan perilaku dan sikap terhadap VCT pada LSL di Sukoharjo. J Kesehatan. 2020;12(2):102-6. doi: 10.23917/jk.v12i2.9766.
8. Gaolathe T, Wirth KE, Holme MP, Makhema J, Moyo S, Chakalisa U. Botswanas progress toward achieving the 2020 UNAIDS 90-90-90 antiretroviral therapy and virological suppression goals: a population based survey. Lancet HIV. 2016;3(5):e221-30. doi: 10.1016/S2352-3018(16)00037-0, PMID 27126489.
9. Oguntibeju OO. Quality of life of people living with HIV and AIDS and antiretroviral therapy. HIV AIDS (Auckl). 2012 Aug 6;4:117-24. doi: 10.2147/HIV.S32321, PMID 22893751.
10. Nugraheni AY, Amelia R, Rizki IF. Evaluasi terapi antiretroviral pasien HIV/AIDS. Farmasetis. 2019;8(2):45-54. doi: 10.32583/farmasetis.v8i2.567.
11. Wahyudi A, Cholisoh Z. Compliance profile of the use of antiretroviral drugs in HIV/AIDS patients in a public hospital in central java in 2022. J Kesehatan Medika Saintika. 2023;14(2).
12. Puspasari D, Wisaksana R, Ruslami R. Adverse drug reactions and compliance with antiretroviral therapy in HIV patients bandung: Hasan Sadikin Hospital 2015. J Sains Dan Kesehatan. 2018;3(4):175-81.
13. World Health Organization. Safety of medicine: adverse drug reactions; 2018. Available from: https://www.who.int/docs/default-source/medicines/safety-of-medicines-adverse-drug-reactions-jun18.pdf?sfvrsn=4fcaf40_2. [Last accessed on 14 Apr 2025].
14. World Health Organization. Consolidated guidelines on HIV testing services. Geneva: World Health Organization; 2015. Available from: http://apps.who.int/iris/bitstream/10665/179870/1/9789241508926_eng.pdf.
15. Micaglio E, Locati ET, Monasky MM, Romani F, Heilbron F, Pappone C. Role of pharmacogenetics in adverse drug reactions: an update towards personalized medicine. Front Pharmacol. 2021 Apr 30;12:651720. doi: 10.3389/fphar.2021.651720, PMID 33995067.
16. Mallal S, Phillips E, Carosi G, Molina JM, Workman C, Tomazic J. HLA-b*5701 screening for hypersensitivity to abacavir. N Engl J Med. 2008;358(6):568-79. doi: 10.1056/NEJMoa0706135, PMID 18256392.
17. Rotger M, Colombo S, Furrer H, Bleiber G, Buclin T, Lee BL. Influence of CYP2B6 polymorphism on plasma and intracellular concentrations and toxicity of efavirenz and nevirapine in HIV infected patients. Clin Pharmacol Ther. 2007 Jan;81(3):557-66. doi: 10.1038/sj.clpt.6100100.
18. Ministry of Health of the Republic of Indonesia. Pedoman Pelayanan Kefarmasian Untuk ODHA. Jakarta: Ministry of Health RI; 2006.
19. Tariq RA, Vashisht R, Sinha A. Medication dispensing errors and prevention. In: Treasure Island, (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519065.
20. Allard NL, MacLachlan JH, Dev A, Dwyer J, Srivatsa G, Spelman T. Adherence in chronic hepatitis B: associations between medication possession ratio and adverse viral outcomes. BMC Gastroenterol. 2020;20(1):140. doi: 10.1186/s12876-020-01219-w, PMID 32381025.

21. Ogston SA, Lemeshow S, Hosmer DW, Klar J, Lwanga SK. Adequacy of sample size in health studies. Biometrics. 1991;47(1). doi: 10.2307/2532527.
22. Mendes JC, Bonolo PF, Ceccato MD, Costa JO, Reis AM, dos Santos H. Adverse reactions associated with first line regimens in patient initiating antiretroviral therapy. Eur J Clin Pharmacol. 2018;74(8):1077-88. doi: 10.1007/s00228-018-2472-y, PMID 29740676.
23. Liver Tox. Clinical and research information on drug induced liver injury. In: Bethesda: National Institute of Diabetes and Digestive and Kidney Diseases; 2012. Adverse Drug Reaction Probability Scale (Naranjo) in Drug Induced Liver Injury. Available from: https://www.ncbi.nlm.nih.gov/books/NBK548069.
24. Eluwa GI, Badru T, Agu KA, Akpoigbe KJ, Chabikuli O, Hamelmann C. Erratum to: adverse drug reactions to antiretroviral therapy (ARVs): incidence type and risk factors in Nigeria. BMC Clin Pharmacol. 2012;12(1):14. doi: 10.1186/1472-6904-12-14.
25. Rukmangathen R, Brahmanapalli VD, Thammisetty DP, Pemmasani D, Gali SD, Atmakuru RB. Study of adverse drug reactions to antiretroviral therapy in a tertiary care hospital Tirupati. Perspect Clin Res. 2020;11(4):158-63. doi: 10.4103/picr.PICR_133_18, PMID 33489833.
26. Khan K, Khan AH, Sulaiman SA, Soo CT, Akhtar A. Adverse drug reactions in HIV/AIDS patients at a Tertiary Care Hospital in Penang, Malaysia. Japan J Infect Dis. 2016;69(1):56-9. doi: 10.7883/yoken.JJID.2014.246, PMID 26073728.
27. Tadesse WT, Mekonnen AB, Tesfaye WH, Tadesse YT. Self-reported adverse drug reactions and their influence on highly active antiretroviral therapy in HIV infected patients: a cross sectional study. BMC Pharmacol Toxicol. 2014;15(1):32. doi: 10.1186/2050-6511-15-32, PMID 24957052.
28. Padua CA, Cesar CC, Bonolo PF, Acurcio FA, Guimaraes MD. High incidence of adverse reactions to initial antiretroviral therapy in Brazil. Braz J Med Biol Res. 2006;39(4):495-505. doi: 10.1590/S0100-879X2006000400010, PMID 16612473.
29. Kumar A, Girish H, Nawaz A, Balu P, Kumar B. Determinants of quality of life among people living with HIV/AIDS: a cross sectional study in central Karnataka, India. Int J Med Sci Public Health. 2014;3(11):1413. doi: 10.5455/ijmsph.2014.230820142.
30. Prosperi MC, Fabbiani M, Fanti I, Zaccarelli M, Colafigli M, Mondi A. Predictors of first line antiretroviral therapy discontinuation due to drug related adverse events in HIV-infected patients: a retrospective cohort study. BMC Infect Dis. 2012;12(1):296. doi: 10.1186/1471-2334-12-296, PMID 23145925.
31. Arisudhana GA, Sofro MA, Sujianto U. Antiretroviral side effects on adherence in PLWHA in central java. Nurse Media J Nurs. 2019;8(2):79. doi: 10.14710/nmjn.v8i2.20742.
32. Barus T. Evaluation of side effects of ARV drugs and their management at penjaringan health center Jakarta, 2013-2015. Soc Clin Pharm Indo J. 2017;2(1):29-37.
33. Zosangpuii C, Datta S, Gunindro N, Meena D, Nameirakpam SS. Adverse drug reaction patterns of anti-retroviral drugs: a study in a tertiary care teaching institute of North East India. Asian J Pharm Clin Res. 2022;15(4):38-41. doi: 10.22159/ajpcr.2022.v15i4.44174.
34. Dua M, Narwat A, Goyal A. Drug induced cutaneous reactions: a pharmacovigilance study. Int J Pharm Pharm Sci. 2024;16(3):26-30. doi: 10.22159/ijpps.2024v16i3.48975.
35. Adiningsih FF, Wilar R, Pongtuluran OB. Efek samping obat antiretroviral regimen TLE pada ODHA di klinik VCT RSUD Jayapura tahun 2023. J Ilmiah Kesehatan Diagn. 2023;17(3):176-83.
36. Handayani D, Lestari N, Pasande A. Gambaran efek samping obat antiretroviral pada pasien HIV/AIDS di RSUD undata palu. Pharmacon J Farmasi Indones. 2021;20(2):124.